

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
V. Sandig, et al.) Group Art Unit: 1633
Application No.: 10/578,043) Examiner: Leavitt, M.G.
Filed: January 9, 2008) Confirmation No.: 5415
For: Immortalized Avian Cell Lines for Virus)
Production)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, WEO DODDIN, hereby declare:

1. I hold a Ph.D. degree in biochemistry and retrovirology and consider myself one of skill in the art of virology.
2. I have published 13 articles indexed in the "PubMed.gov" NCBI library.
3. I have reviewed the claims of U.S. Application No. 10/578,043, and I have been informed that these claims are rejected on the basis of obviousness, that one of skill in the art would have recognized that the results of the combination of E1A and E1B genes would have yielded the predictable results of inducing cell proliferation by disrupting Rb/E2F complexes and inactivating p53 in avian cells, purely due to their known interaction and activity in human and mammalian cells.

4. I disagree with the Office Action's assertion. I am of the view that the immortalization of avian cells with E1A and E1B 55K from mastadenoviruses is an unexpected result.

5. The inventors have observed that human adenoviruses cannot replicate in avian cells. However, the inventors noticed that human adenoviruses can successfully enter avian cells. Thus, the lack of replication is not due to the fact that said adenoviruses do not find the correct receptors for viral entry. It is predicted that the viral regulatory pathways within the avian cell, which include E1A and E1B 55K, appear to be dysfunctional when compared to human and mammalian cells.

6. It is clear that human p53 and avian p53 share very few conserved amino acid sequences. I have looked at the human and chicken p53 protein sequences. The sequence identity between human p53 (amino acid sequence according to Annex I enclosed herewith) and chicken p53 (amino acid sequence according to Annex II enclosed herewith) is only 53.7% (see sequence alignment between the whole length human p53 and chicken p53 of Annex III enclosed herewith). Moreover, the sequence identity between the N-terminal transactivation domain (amino acids 1 to 58) of human p53 which is bound by E1B 55K of human adenovirus and rendered inactive and chicken p53 is only 29.9% (see sequence alignment between the N-terminal transactivation domains of human p53 and chicken p53 of Annex IV enclosed herewith).

7. Due to this difference in amino acid sequence, the binding activity of avian p53 cannot be predicted by human p53 results. Thus, it is unknown whether the E1A and E1B proteins will have the same immortalization effect, or any effect, on avian cells.

8. Considering the above, the skilled person in the art would have not expected that E1A and E1B 55K from mastadenoviruses would have the same activity in avian cells than in mammalian cells, i.e. that E1A and E1B 55K from mastadenoviruses can also affect the avian homologues of Rb, E2F and p53.

9. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. All of the statements I made herein are made of my own volition. I understand that willful false statements may subject me to fines, imprisonment or both, pursuant to Section 1001 of Title 18 of the United States Code.

Signed: 
Date: 05 September 2011

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Protein

Translations of Life

Display Settings: GenPept

P53 [Homo sapiens]

GenBank: BAC16799.1

EASTA: Graphics

Gene

LOCUS BAC16799 393 aa linear PRI 01-APR-2003
 DEFINITION P53 [Homo sapiens].
 ACCESSION BAC16799
 VERSION BAC16799.1 GI:23491729
 DBSOURCE accession AB082923.1
 KEYWORDS
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Euarchontoglires; Primates; Homlorrhini;
 Catarrhini; Hominidae; Homo.
 REFERENCE 1
 AUTHORS Azuma, R., Shichijo, S., Maeda, Y., Nakatsura, T., Nonaka, Y., Fujii, T.,
 Koike, K. and Itoh, K.
 TITLE Mutated p53 gene encodes a nonmutated epitope recognized by
 HLA-B*4601-restricted and tumor cell-reactive CTLs at tumor site
 JOURNAL Cancer Res. 63 (4), 854-858 (2003)
 PUBMED 12551737
 REFERENCE 2 (residues 1 to 393)
 AUTHORS Shichijo, S. and Itoh, K.
 TITLE Direct Submission
 JOURNAL Submitted (26-MAR-2002) Shigeaki Shichijo, Kurume Univ. School of
 Med., Dep. Immunol., 67-Asahi-nachi, Kurume, Fukuoka 830-0011,
 Japan (E-mail: shichijo@med.kurume-u.ac.jp, Tel:81-942-31-7551,
 Fax:81-942-31-7699)
 FEATURES Location/Qualifiers
 source 1..393
 /organism="Homo sapiens"
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 Protein 1..393
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 Site order(177..179,181)
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 181 rrsadqgiap pqmlirvegn lrveylddm tfrhsvvvpv eppavgsdtt tihynymns
 241 scnggnwrrp ilttitleds agalgrnsf evuvcaepgr orrtteewnlr kkgephbelp
 301 pgatckraln ntssspqhk xplidgevfti qirgrefsm frlnealei xdagakrge
 361 geratashhik skkggstsxn kklnfktteg ded

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Amex E

Protein

Translations of Life

Display Settings: GenPept

RecName: Full=Cellular tumor antigen p53; AltName: Full=Tumor suppressor p53

Swiss-Prot: P10360.1

FASTA Graphics

Gene

LOCUS P53_CHICK 367 aa linear VRT 30-MOV-2010
 DEFINITION RecName: Full=Cellular tumor antigen p53; AltName: Full=Tumor suppressor p53.
 ACCESSION P10360
 VERSION P10360.1 GI:129368
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 created: Jul 1, 1993.
 sequence updated: Jul 1, 1993.
 annotation updated: Nov 30, 2010.
 xrefs: X13057_1, CAA31456_1, S02193, NP_990595_1
 xrefs (non-sequence databases): IPI:IP10360129, UniGene:Gga_706,
 ProteinModelPortal:P10360, SMR:P10360, GeneID:396299,
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 GO:0005314, GO:0001571, GO:0001722, GO:0008270, GO:0006151,
 GO:0007049, GO:0031006, GO:0004155, GO:0002347, GO:0007150,
 InterPro:IPR008987, InterPro:IPR012346, InterPro:IPR015651,
 InterPro:IPR011615, InterPro:IPR019391, InterPro:IPR007117,
 Gene3D:G3DSA:2_60_40_720, Gene3D:G3DSA:4_10_170_10,
 PANTHER:PTM011447, Pfam:PP000870, Pfam:PP07110, PRINTS:PR00366,
 SUPERFAM:SSF49417, CUFFPAM:SSF47719, PROSITE:PS00348
 KEYWORDS Activator; Apoptosis; Cell cycle; Cytoplasm; DNA-binding;
 Metal-binding; Nucleus; Phosphoprotein; Transcription;
 Transcription regulation; Tumor suppressor; Zinc.
 SOURCE Gallus gallus (chicken)
 ORGANISM Gallus gallus
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Archosauria; Dinosauria; Saurischia; Theropoda; Coelurosauria;
 Aves; Neognathae; Galliformes; Phasianidae; Phasianinae; Gallus.
 REFERENCE 1 (residues 1 to 367)
 AUTHORS Soussi,T., Begue,A., Kress,M., Stehelin,D. and May,P.
 TITLE Nucleotide sequence of a cDNA encoding the chicken p53 nuclear oncoprotein
 JOURNAL Nucleic Acids Res. 16 (23), 11383 (1988)
 PUBMED 3009851
 REMARK NUCLEOTIDE SEQUENCE (NRNND).
 STRAIN=SFAPAS
 COMMENT On Apr 12, 2005 this sequence version replaced gi:36220.
 [FUNCTION] Acts as a tumor suppressor in many tumor types, induces growth arrest or apoptosis depending on the physiological circumstances and cell type. Involved in cell cycle regulation as a trans-activator that acts to negatively regulate cell division by controlling a set of genes required for this process. One of the activated genes is an inhibitor of cyclin-dependent kinases. Apoptosis induction seems to be mediated either by stimulation of BAX and FAS antigen expression, or by repression of Bcl-2 expression (By similarity).
 [COFACTOR] Binds 1 zinc ion per subunit (By similarity).
 [SUBUNIT] Binds DNA as a homotrimer (By similarity).
 [SUBCELLULAR LOCATION] Cytoplasm (By similarity). Nucleus (By similarity).
 [SIMILARITY] Belongs to the p53 family.
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 Gene 1..367
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 Protein 1..367
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Region 286..302
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similarity)."
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/note="Nuclear export signal (By similarity)."
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241 lcleppggql lgrxcfevrv cacpgdzki eeeufhkrge aggvakramw poteapeppk
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Answer 2

EMBOSS Home Help General Help Formats Gaps Matrix References EMBOSS-Align Help	<input type="button" value="All Databases"/> <input type="text" value="Enter Text Here"/> <input type="button" value="Go"/>											
	Databases	Tools										
	EBI Groups	Training										
	Industry	About Us										
	Help	Help										
	EMBOSS	Align Results										
	EMBOSS Align Results											
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Matrix	Blosum62											
Open gap penalty	10.0											
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<http://www.ebi.ac.uk/Tools/es/cgi-bin/jobresults.cgi/needle/needle-20101223-080918...> 23.12.2010

EBI

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EMBOSS Align Results

Needle Results	
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Open gap penalty	10.0
Gap extension penalty	0.5
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SUBMIT ANOTHER JOB

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#   -sprotein2
#   -auto
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# Extend_penalty: 0.5
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# Length: 67
# Identity: 20/67 (29.9%)
# Similarity: 27/67 (40.3%)
# Gaps: 18/67 (26.9%)
# Score: 64.0
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#####

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terminal/trans-
lation domain
no segments

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EMBOSS_001: .: .	46

terminal/trans-
lation domain
w/stop

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EMBOSS_001	..	
EMBOSS_001	46 ----psdpppppppppl	58

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#
#-----
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